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EXAMINER

FORMAN, BETTY J

ART UNIT PAPER NUMBER

1634

DATE MAILED: 03/31/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/616,849

Applicant(s)

BURCHARD, JULJA

Examiner

BJ Forman

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 06 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 27-30 is/are pending in the application.
- 4a) Of the above claim(s) 27-30, 33-40, 42-54, 59-68, 73-75, 84, 85 and 90-104 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 27-30, 33-40, 42-54, 59-68, 73-75, 84, 85 and 90-104 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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## **DETAILED ACTION**

### ***Status of the Claims***

1. This action is in response to Appeal Brief filed 6 January 2004.

The previous rejections in the Office Action dated 7 April 2003, not reiterated below, are withdrawn in view of new grounds for rejection.

Applicant's arguments presented in the Appeal Brief have been thoroughly reviewed and are discussed below as they apply to the current grounds for rejection. New grounds for rejection are discussed.

Claims 26-30, 33-40, 42-54, 59-68, 73-75, 84-85, 90-104 are under prosecution.

### ***Claim Rejections - 35 USC § 102***

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 27-30, 33-36, 38, 40, 43-54, 59-60, 64-65, 67-68, 73, 90-91, 93, 95-104 are rejected under 35 U.S.C. 102(b) as being anticipated by Lo et al (U.S. Patent No. 4,900,659, issued 13 February 1990).

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Regarding Claim 27, Lo et al disclose a method for evaluating a polynucleotide probe comprising determining a ratio of the amount of hybridization of polynucleotides in a first sample to the probe and the amount of hybridization of polynucleotides in a second sample to the probe wherein the first sample comprises a plurality of molecules comprising the target chromosomal DNA e.g. strain 53414 (Column 8, lines 13-28) and the second sample comprises a plurality of different polynucleotides (i.e. chromosomal DNA from *N. meningitidis*, strains 53415, 53416, 53417, 53418 and 53419 and chromosomal DNA from *N. gonorrhoeae*, 53420, 53421, 53422, 53423, 53424, 53425) wherein at least 75% of the polynucleotide molecules in the first sample comprise the target sequence i.e. the molecules in the first sample comprise chromosomal DNA from strain 53414 (i.e. the target sequence) (Claim 1). Furthermore, Lo et al teach the method whereby a binding property (i.e. target specificity) of the probe is evaluated (Column 3, lines 30-39).

Lo et al teach preparation of samples comprising chromosomal DNA from different *N. meningitidis*, strains and from different *N. gonorrhoeae*, strains. The samples are each, separately spotted onto filter whereby the spot comprising the first sample contains *N. gonorrhoeae* chromosomal DNA and therefore comprises the target i.e. *N. gonorrhoeae* chromosomal DNA. The spots are each contacted with predetermined nucleotide sequence probes wherein the probes are predetermined as being fragmented chromosomal DNA from *N. gonorrhoeae* and to have preferably about 256 base pairs, but more than 12 (Column 5, lines 15-66). As such, Lo et al teach the claimed invention (Column 10, line 51-Column 12, line 65).

Regarding Claim 28, Lo et al disclose the method wherein the probe is complementary to at least a hybridizable portion of the target (Column 9, line 31-Column 10, line 50).

Regarding Claim 29, Lo et al disclose the method wherein the target in the first sample is a sequence of a gene from an organism i.e. *N. gonorrhoeae* chromosomal DNA (Column 4, line 44-Column 5, line 65). It is noted that the claim recites "a nucleotide sequence of a gene".

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The claim does not require the target be a complete gene or transcript but instead merely requires a sequence of a gene. Furthermore, the claim recites, "probe to a target" but does not require the probe comprises a complete target. As such, the hybridization of fragmented chromosomal DNA to chromosomal DNA taught by Lo et al meets the limitations of the claim.

Regarding Claim 30, Lo et al disclose the method wherein the polynucleotide molecules in the second sample comprise sequences of a plurality of genes of an organism (i.e. chromosomal DNA, Column 8, line 13-Column 9, line 17).

Regarding Claims 33-35, Lo et al disclose the method wherein at least 99% of the polynucleotides in the first sample comprise the target sequence e.g. chromosomal DNA from *N. gonorrhoeae* (Column 8, lines 13-28).

Regarding Claim 36, Lo et al disclose the method wherein the second sample does not comprise the target (i.e. chromosomal DNA from *N. gonorrhoeae*) but instead comprises chromosomal DNA from *N. meningitides* (Column 8, lines 13-28).

Regarding Claim 38, Lo et al disclose the method wherein the second sample comprises polynucleotides comprising the target and a plurality of different molecules comprising a different sequence, not the target. Lo et al teach the second sample comprises chromosomal DNA from different *N. meningitides* strains and from *N. gonorrhoeae* strains (Column 8, lines 13-28). Lo et al teach that the *N. meningitides* strains do not comprise the target while the *N. gonorrhoeae* strains do comprise the target as evidenced by the *N. gonorrhoeae* detection taught by Lo et al (Column 10, line 51-Column 12, line 65).

Regarding Claim 40, Lo et al disclose the method wherein the first sample further comprises molecules that do not comprise the target e.g. chromosomal regions homologous between *N. meningitides* and *N. gonorrhoeae* (Column 3, lines 10-30) and the second sample lacks molecules comprising the target i.e. the second sample comprises organism-specific chromosomal DNA i.e. DNA from *N. meningitides* and not having chromosomal DNA from *N. gonorrhoeae* (i.e. target, Column 8, lines 13-28).

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Regarding Claims 43-47, Lo et al disclose the method wherein the first sample further comprises molecules that do not comprise the target e.g. chromosomal regions homologous between *N. meningitides* and *N. gonorrhoeae* (Column 3, lines 10-30) and the second sample comprises polynucleotides comprising the target and a plurality of different polynucleotides comprising different sequences, not the target. In this embodiment the first and second samples each comprises sample spots of *N. meningitides* and sample spots of *N. gonorrhoeae* wherein the first sample spots have 500 nanograms chromosomal DNA and the second sample spots have 5 picograms of chromosomal DNA thereby providing amounts of polynucleotides differing by at least a factor of 100 (Column 11, lines 29-42). The open claim language "comprising" encompasses the first sample having polynucleotide not having the target i.e. *N. meningitides*.

Regarding Claim 48-54, Lo et al teaches the probe evaluation method wherein the amount/abundance of polynucleotide in the first sample is the same as the amount/abundance in the second sample (Column 11, lines 29-42) and therefore differs by no more than a factor of two or by no more than 1% as claimed.

Regarding Claim 59, Lo et al disclose the method wherein the polynucleotides in the first sample are detectably labeled (Column 11, lines 43-65).

Regarding Claim 60, Lo et al disclose the method wherein the polynucleotides in the first sample are detectably labeled (Column 11, lines 43-65).

Regarding Claim 64, Lo et al disclose the method wherein the polynucleotide probe is attached to the surface of the support i.e. via hybridization to the immobilized chromosomal DNA (Column 8, lines 50-65).

Regarding Claim 65, Lo et al disclose the method wherein the probe is one of a plurality of probes (Column 9, line 14-Column 10, line 50).

Regarding Claim 67, Lo et al disclose a method for evaluating a plurality of polynucleotide probes comprising a predetermined sequence. The method comprising

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determining a ratio of the amount of hybridization of polynucleotides in a first sample to the probe and the amount of hybridization of polynucleotides in a second sample to the probe wherein the first sample comprises a plurality of molecules comprising the target chromosomal DNA e.g. strain 53414 (Column 8, lines 13-28) and the second sample comprises a plurality of different polynucleotides (i.e. chromosomal DNA from *N. meningitidis*, strains 53415, 53416, 53417, 53418 and 53419 and chromosomal DNA from *N. gonorrhoeae*, 53420, 53421, 53422, 53423, 53424, 53425) wherein at least 75% of the polynucleotide molecules in the first sample comprise the target sequence i.e. the molecules in the first sample comprise chromosomal DNA from strain 53414 (i.e. the target sequence) (Claim 1).

Lo et al teach preparation of samples comprising chromosomal DNA from different *N. meningitidis*, strains and from different *N. gonorrhoeae*, strains. The samples are each, separately spotted onto filter whereby the spot comprising the first sample contains *N. gonorrhoeae* chromosomal DNA and therefore comprises the target i.e. *N. gonorrhoeae* chromosomal DNA. The spots are each contacted with predetermined nucleotide sequence probes wherein the probes are predetermined as being fragmented chromosomal DNA from *N. gonorrhoeae* and having preferably about 256 base pairs, but more than 12 (Column 5, lines 15-66). As such, Lo et al teach the claimed invention (Column 10, line 51-Column 12, line 65).

Regarding Claim 68, Lo et al disclose the method wherein the probe is complementary to at least a hybridizable portion of the target (Column 9, line 31-Column 10, line 50).

Regarding Claim 73, Lo et al disclose the method wherein the polynucleotide probes are attached to the surface of the support i.e. via hybridization to the immobilized chromosomal DNA (Column 8, lines 50-65).

Regarding Claim 90, Lo et al disclose the method wherein the polynucleotides molecule comprising the target are the same i.e. chromosomal DNA from *N. gonorrhoeae* (Columns 5-6).

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Regarding Claim 91, Lo et al disclose a method for evaluating a plurality of polynucleotide probes comprising a predetermined sequence. The method comprising determining a ratio of the amount of hybridization of polynucleotides in a first sample to the probe and the amount of hybridization of polynucleotides in a second sample to the probe wherein the first sample comprises a plurality of molecules comprising the target chromosomal non-homologous DNA and a plurality of molecules that do not comprise the target i.e. homologous DNA (Column 3, lines 10-30) and the second sample comprises a plurality of different polynucleotides and do not comprise the target (i.e. chromosomal DNA from *N. meningitidis*, strains 53415, 53416, 53417, 53418 and 53419 (Column 8, lines 9-49) wherein each probe comprises a predetermined sequence Column 5, lines 18-65). Lo et al teach the probes are predetermined nucleotide sequences wherein the probes are predetermined as being fragmented chromosomal DNA from *N. gonorrhoeae* and having preferably about 256 base pairs, but more than 12 (Column 5, lines 15-66). As such, Lo et al teach the claimed invention (Column 10, line 51-Column 12, line 65).

Lo et al further teach the hybridization ratio is used as a measure of the binding property (Column 12, lines 10-65 and Claim 1).

Regarding Claim 93, Lo et al disclose a method for evaluating a plurality of polynucleotide probes comprising a predetermined sequence. The method comprising determining a ratio of the amount of hybridization of polynucleotides in a first sample to the probe and the amount of hybridization of polynucleotides in a second sample to the probe wherein the first sample comprises a plurality of molecules comprising the target chromosomal non-homologous DNA and a plurality of molecules that do not comprise the target i.e. homologous DNA (Column 3, lines 10-30) and the second sample comprises a plurality of different polynucleotides (i.e. chromosomal DNA from *N. meningitidis*, strains 53415, 53416, 53417, 53418 and 53419 (Column 8, lines 9-49) wherein each probe comprises a predetermined sequence Column 5, lines 18-65). Lo et al teach the probes are predetermined



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nucleotide sequences wherein the probes are predetermined as being fragmented chromosomal DNA from *N. gonorrhoeae* and having preferably about 256 base pairs, but more than 12 (Column 5, lines 15-66). As such, Lo et al teach the claimed invention (Column 10, line 51-Column 12, line 65).

Lo et al further teach the hybridization ratio is used as a measure of the binding property (Column 12, lines 10-65 and Claim 1).

Regarding Claims 95-99, Lo et al disclose the method wherein the first sample further comprises molecules that do not comprise the target e.g. chromosomal regions homologous between *N. meningitides* and *N. gonorrhoeae* (Column 3, lines 10-30) and the second sample comprises polynucleotides comprising the target and a plurality of different polynucleotides comprising different sequences, not the target. In this embodiment the first and second samples each comprises sample spots of *N. meningitides* and sample spots of *N. gonorrhoeae* wherein the first sample spots have 500 nanograms chromosomal DNA and the second sample spots have 5 picograms of chromosomal DNA thereby providing amounts of polynucleotides differing by at least a factor of 100 (Column 11, lines 29-42). The open claim language “comprising” encompasses the first sample having polynucleotide not having the target i.e. *N. meningitides*.

Regarding Claims 100-104, Lo et al teaches the probe evaluation method wherein the amount/abundance of polynucleotide in the first sample is the same as the amount/abundance in the second sample (Column 11, lines 29-42) and therefore differs by no more than a factor of two of by no more than 1% as claimed

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***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 37, 39, 42, 92 and 94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lo et al (U.S. Patent No. 4,900,659, issued 13 February 1990).

Regarding Claims 37, 39, 42, 92 and 94 Lo et al disclose a method for evaluating a polynucleotide probe comprising determining a ratio of the amount of hybridization of polynucleotides in a first sample to the probe and the amount of hybridization of polynucleotides in a second sample to the probe wherein the first sample comprises a plurality of molecules comprising the target chromosomal DNA e.g. strain 53414 (Column 8, lines 13-28) and the second sample comprises a plurality of different polynucleotides (i.e. chromosomal DNA from *N. meningitidis*, strains 53415, 53416, 53417, 53418 and 53419 and chromosomal DNA from *N. gonorrhoeae*, 53420, 53421, 53422, 53423, 53424, 53425) wherein at least 75% of the polynucleotide molecules in the first sample comprise the target sequence i.e. the molecules in the first sample comprise chromosomal DNA from strain 53414 (i.e. the target sequence) (Claim 1).

Furthermore, Lo et al teach their method screens closely related samples to analyze probe-specific probes (Column 3, lines 30-39) wherein their method provides for screening nucleotide sequences that are specific for a "genetically distinct group" (Column 4, lines 15-17 and 18-42). Which clearly suggests their method is useful for wild-type and mutants (e.g. deletion mutants). Hence, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the method of Lo et al to screen genetically distinct groups (e.g. mutants and/or wild-type samples) to thereby screen and analyze mutants

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and/or wild-type-specific probes as they suggest (Column 3, lines 30-39 and Column 4, lines 15-17).

7. Claims 61-63, 66, 74-75, 84-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lo et al (U.S. Patent No. 4,900,659, issued 13 February 1990) in view of Lockhart et al (U.S. Patent No. 6,344,316 B1, filed 25 June 1997).

Regarding Claims 61-63, 66, 74-75, 84-85, Lo et al teach the methods of probe analysis as detailed above wherein the polynucleotide probes are detectably labeled (Column 11, lines 43-65) but they do not teach the polynucleotides are differentially labeled with fluorescent labels and they do not teach the probes are in an array of probes wherein different probes are attached to different locations on the array.

However, Lockhart et al teach a similar method for evaluating a binding property of a polynucleotide probe comprising a predetermined nucleotide sequence to a target nucleotide sequence, said method comprising: comparing the amount of hybridization of polynucleotide in a first sample to the probe with the amount of hybridization of polynucleotides in a second sample to the probe wherein the first sample comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence and said second sample comprises a plurality of different polynucleotide molecules wherein each different polynucleotide comprises a sequence that is different from the sequences of other polynucleotides and wherein at least 75% of the polynucleotides in the first sample are polynucleotides comprising said target sequence thereby evaluating said binding property of said probe wherein each different polynucleotide in the second sample does not comprise the target sequence wherein the target sequence is a gene sequence and wherein the probes comprise perfect match and mismatch probes (Column 36,

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lines 24-47 and Example 1, Column 70, line 58-Column 73, line 46) wherein different probes are attached to different locations on the array wherein cross-hybridization is minimized (Column 37, line 44-56) and whereby a high-density array of probes are optimized (Column 36, lines 25-27). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the probe array of Lockhart et al to the probe analysis of Lo et al for the obvious benefits of optimizing a high-density array of probes as desired by Lockhart et al (Column 36, lines 25-27).

Lockhart et al further teach fluorescent labeling wherein different samples are differentially labeled (Column 24, lines 54-67). Lockhart further provide motivation for using their fluorescent labeling as cited below:

A fluorescent label is preferred because it provides a very strong signal with low background. It is also optically detectable at high resolution and sensitivity through a quick scanning procedure. The nucleic acid samples can all be labeled with a single label, e.g., a single fluorescent label. Alternatively, in another embodiment, different nucleic acid samples can be simultaneously hybridized where each nucleic acid sample has a different label. For instance, one target could have a green fluorescent label and a second target could have a red fluorescent label. The scanning step will distinguish sites of binding of the red label from those binding the green fluorescent label. Each nucleic acid sample (target nucleic acid) can be analyzed independently from one another.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to fluorescently label the different polynucleotides of Lo et al for the expected benefits of providing a very strong signal with low background which is also optically detectable at high resolution and sensitivity through a quick scanning procedure as taught by Lockhart et al (Column 24, lines 54-57). It would have been further obvious to differentially label the different polynucleotides of Lo et al to thereby provide for independent analysis of simultaneously hybridized polynucleotides as taught by Lockhart et al (Column 24, lines 59-67).


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**Conclusion**

8. No claim is allowed.
9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
BJ Forman, Ph.D.  
Primary Examiner  
Art Unit: 1634  
March 29, 2004

  
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